CARDIOVASCULAR, PHARMACOLOGY and CHEMISTRY

NO. 626

CF. #495

Activated: 7/1/66

CF. #344 - 1962-'64

COMPARE:
#33 - 1955 - 1957
#160 - 1957
#213 -1959 - 1961
#301 -1961 - 1962

THE COUNCIL FOR TOBACCO RESEARCH - U.S.A.

COMMITTEE:
Dr. Bing, Chm.
Dr. Cattell
Dr. Jacobson

633 THIRD AVENUE
NEW YORK, N. Y. 10017

Application For Research Grant

Date: June 23, 1967

1. Name of Investigator(s): (include Title and Degrees) Walter Redisch, M.D., Assoc. Prof. Clin. Med., NYU School of Med.; Res. Assoc. NYU Res. Service, Goldwater Mem. Hosp., Welfare Island, N.Y.
E.N. Terry, M.D., Res. Fellow, NYU Res. Service, Goldwater Mem Hosp., Welfare Island, N.Y.

2. Institution & Address:
New York University Research Service, Goldwater Memorial Hospital, Welfare Island, N.Y.
New York University Medical Center, 550 First Avenue, New York, N.Y.

3. Short Title of Project:
(The effect of cigarette smoking on peripheral blood flow in patients with essential hypertension, untreated and treated)

4. Proposed Starting Date: October 1, 1967

5. Anticipated Duration of this Specific Study: One year

6. Brief Description of Objectives or Specific Aims:
It is suggested that the effect of cigarette smoking be studied and compared in the following groups:

1) patients with primary hypertension who have not been treated before and are not being treated while the study is in progress
2) patients with primary hypertension treated with reserpine
3) patients with primary hypertension treated with thiazide
4) patients with a primary hypertension treated with reserpine thiazide combination
5) patients with primary hypertension treated with guanethedin
6) normotensive subjects

Each group to consist of 5 subjects.

Essential hypertension for the purposes of this study is defined as a sustained diastolic pressure of 100 mm Hg or higher without detectable underlying cause.

7. Give a Brief Statement of your Working Hypothesis:

Appended A.

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8. Details of Experimental Design and Procedures: (Attach Separate Pages)

The method to be used in this study is differential venous occlusion plethysmography.

Plethysmographic measurements of the foot and calf are taken, those of the foot being representative of skin blood flow while measurements of the calf are representative of muscle blood flow. The calf and foot are placed in the appropriate plethysmographic lucite chambers. The chambers are then made airtight with vaseline and foam rubber. Volume changes of the limb are calculated from the effect of a known volume, namely 5 ml air injected into the chamber, has on the deflection of the recorder. On the recording a time-scale permits measurement of the distance equivalent to 10 seconds on the base line. At this point a perpendicular is erected. Blood flow in ml/minute in 100 cc of tissue is calculated from the formula:

$$\frac{600 \times L}{K \times V} = \text{Blood Flow (ml per minute per 100 ml of tissue)}$$

L is the perpendicular rise of the slope in mm, during 10 seconds. K is the calibration constant of the recording apparatus in mm deflection per ml of change in volume. V is the volume of the enclosed calf or foot in ml which is determined by the water displacement overflow method. (cont'd) Appended B

9. Physical Facilities Available (Where Other than Administering Organization Indicate Geographical Location)

New York University Research Laboratories, Goldwater Memorial Hospital, Welfare Island, N.Y. Vascular Research Laboratory, New York University Medical Center, 550 First Ave., N.Y.

10. Additional Requirements:

None

11. Biographical sketches of all principal and professional personnel (append)

Appended D

12. List of publications: (Five most recent as pertinent) (append)

Appended C

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13. Budget: (1st year)

	% time	Amount
A. Salaries (Personnel by names)		
Professional		
Larry Rouen Research Technician	80%	$ R
Guillermo Cortes Research Technician	80%	
Employees Fringe Benefits		
Technical		
	Sub-Total	R
B. Consumable Supplies (list by categories)		
Mercury strain gauges ..... $325.		
Filters, gauge elements and other parts for Constant Temperature Room equipment which needs periodic replacements ..... 175.		
Batteries, elements, paper and ink for Speedomax and Plethysmograph recording 100	Sub-Total	1,000.
Photographic equipment for follow of microvasculature ..... 400.		
C. Other Expenses (itemize)		
Travel (domestic)		
To attend Scientific Meetings	Sub-Total	500.
D. Permanent Equipment (itemize)		
None		None
E. Overhead (15% of A+B+C)		2.191.
	Total	$16,795.

Estimated Future Requirements:

	Salaries	Consumable Suppl.	Other Expenses	Permanent Equip.	Overhead	Total
Year 2						
Year 3						

It is understood that the applicant and institutional officers in applying for a grant have read and found acceptable the Council's "Statement of Policy Containing Conditions and Terms Under Which Project Grants Are Made."

Signature [signature] Director of Project

688-3500 Ext 507 Telephone

Signature Business Officer of the Institution

Telephone

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Other Sources of Financial Support

List financial support for research from all sources, including own institution, for this and/or related research projects.

	Title of Project	Source	Amount	Duration
Current	Vascular Research Fund	SKF and Arlidin	4,000.	Indef.
	Role of Catecholamines in Vasoconstriction	USPHS	30,358.	6/1/67-5/31/68
	Microcirculation in Systemic Rheumatic Disease	USPHS	10,421. to ---	9/1/67
Pending				

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A

THE COUNCIL FOR TOBACCO RESEARCH - U.S.A.

Application For Research Grant

Dr. Walter Redisch
New York University School of Medicine
New York University Research Service

7. Give a Brief Statement of your Working Hypothesis:

There is no proof that cigarette smoking and tobacco smoking in general have the same effects on various physiologic parameters. There is likewise no definite proof that these effects are due to nicotine. However, the effects of cigarette smoking on the cardio-vascular system show some essential similarities to the pharmacologic effects of nicotine.

The pharmacologic action of nicotine consists of a primary transient stimulation and secondary more persistent depression of all sympathetic and parasympathetic ganglia. This includes the adrenal medulla and epinephrine is thereby discharged. Nicotine and tobacco smoking have also been shown to exert an antidiuretic action. This effect is thought to be the result of stimulation and of the supraoptical-hypophyseal system with the subsequent release of posterior pituitary anti-diuretic hormones. Nicotine also markedly stimulates the central nervous system which is particularly evident for the respiratory and vasomotor centres of the medulla. Due to the multiple sites of action one may encounter initially a slowing of the heart rate due to stimulation of the central vagal nuclei and cardiac vagal ganglia. Later owing to the stimulation of sympathetic ganglia, and the central vasomotor centre, tachycardia and a peripheral vasoconstriction may become prominent.

After the stage of sympathetic ganglionic stimulation is succeeded by paralysis, smaller vessels of the periphery, especially those of the skin may dilate.

These responses should be studied to ascertain the presence or absence of an increased catecholamine activity in the systemic blood vessels of patients with hypertension and the presence or absence of a basic abnormality in catecholamine metabolism in primary hypertension. Such findings in untreated patients with primary hypertension should be compared to findings in patients treated with various drugs to lower blood pressure. Also the effect of cigarette smoking on the treatment of hypertension with diuretics should be studied.

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B

THE COUNCIL FOR TOBACCO RESEARCH - U.S.A.

Application For Research Grant

Dr. Walter Redisch
New York University School of Medicine
New York University Research Service

8. Details of Experimental Design and Procedures: (cont'd)

When measuring blood flow through the calf (i.e. muscle vascular bed) two pressure cuffs are applied to the extremity to be measured. The distal (occlusion) cuff is inflated to 270 mm Hg, the one proximal to the plastic case (collecting cuff) to the individual's diastolic blood pressure minus 10 mm Hg. When measuring blood flow to the foot (i.e skin vascular bed) only the collecting cuff is used which is inflated to the individual's diastolic blood pressure minus 10 mm Hg. Following sudden occlusion, the linear portion of the rising slope of the recorded curve is used to calculate the rate of flow according to the formula mentioned above.

All experiments of course will be done in a constant temperature laboratory, at temperatures of 20 and 28°C. Humidity will be held constant at 55%.

In order to avoid environmental influences, patients in basal state will be brought to the constant temperature laboratory where they will rest on a bed while quasi-continuously the skin temperature on both big toes and the right middle finger are recorded using a six channel Speedomax. A patient is considered to be adjusted to the environment of the room when the skin temperature of his toes and fingers has come down to constant room temperature and stayed there for thirty minutes. In patients whose skin temperature does not come down to room temperature despite prolonged exposure, maintenance of a constant skin temperature of toes and fingers for 30 minutes is considered to represent adaptation.

For smoking, our standard procedure will be used, subjects will be instructed and supervised to smoke at the rate of one inhalation every thirty seconds for six minutes (total of twelve inhalations).

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C

THE COUNCIL FOR TOBACCO RESEARCH - U.S.A.

Application For Research Grant

Dr. Walter Redisch
New York University School of Medicine
New York University Research Service

12. Publications

Studies in Tobacco Hypersensitivity.
Fontana, V.J., Redisch, W , Nemir, R., Smith, M.K., DeCrinis, K. and Sulzberger, M.B.
J. of Allergy, 30: 241, 1959.

Tobacco Hypersensitivity: Peripheral Circulatory Implications.
Walter Redisch, M.D.
Presented at the New York Academy of Sciences, March 25, 1960.
Annals, N.Y. Acad. of Sciences 90: Art. 1, 142-144, Sept. 27, 1960.

Vascular Responses to Smoking Tobacco Compared with Responses to Skin Testing of Tobacco Extracts.
DeCrinis, K., Redisch, W., Fontana, V., Lewis, A., Sulzberger, M.B. and Steele, J.M.
Annals Int. Med. 52: No. 5, 1960.

Tobacco Allergy and Vascular Responses.
Redisch, W.
Reprinted from BOOK - TOBACCO AND HEALTH, James and Rosenthal, et al..
Charles C. Thomas, Publisher, Springfield, Illinois, pp. 352, 1962.

Studies on Effects of Catecholamines Upon Extremity Blood Flow in Man.
Redisch, W.
Metabolismus Parietis Vasorum - Praha Diebus - 4 - 9 September 1961.

Evaluation of Vascular Responses to Cigarette Smoking.
Redisch, W., Messina, E.J., Terry, E.N., Rouen, L.R. and Steele, J.M.
Submitted for publication, 1967, Angiology. (Accepted 7/27/67)

A Manifestation of Diabetic Microangiopathy in Nailfold Capillaries.
Terry, E.N., Messina, E.J., Schwartz, M.S., Redisch, W. and Steele, J.M.
Diabetes, in press.

Blood Flow Measurements in Response to Bamethane Sulfate in Man.
Terry, E.N., Messina, E.J., Redisch, W. and Steele, J.M.
Angiology 18: 161-173, March 1967.

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R: REDACTED MATERIAL

D

CURRICULUM VITAE

Name: Walter Redisch, M.D., F.A.C.P., F.R.S.A.

Address: R

Date and Place of Birth: R Prague, Bohemia

Marital Status: R

Former Appointments:

Demonstrator, Dept. of Physiol., German University of Prague 1921-38

Fellowship, Heart Station, Vienna University 1927

Fellowship, Dept. of Internal Medicine, Franz Joseph's Hospital, Vienna 1929

Fellowship, Dept. of Internal Medicine, University of Tuebingen, Tubingen, Germany 1924

University Ass't., Dept. of Gen. and Exp. Path. and Clin. Propedeutics, German University Med. School of Prague and Univ. Hospital 1923-32

Present Appointments:

Associate Professor of Clinical Medicine, New York University School of Medicine, New York, NY

Research Associate, New York University Research Service, Goldwater Memorial Hospital, New York, NY (Director, Dr. J. Murray Steele)

Visiting Physician, New York University Medical Research Division, Goldwater Memorial Hospital, New York, NY

Associate Visiting Physician, Bellevue Hospital, New York, NY

Associate Attending Physician, University Hospital, New York, NY

Physician-in-charge, Vascular Section, New York University Cardiovascular Clinic, Bellevue Hospital.

Physician-in-charge, Medical-Surgical Vascular Group, New York University Medical Center (Surgeon-in-charge, Dr. Roy Clauss)

Member, Advisory Board, Council on Circulation, A.H.A.

Consultant, Vascular Disease, St. Michael's Hospital, Newark, New Jersey.

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Curriculum Vitae
Walter Redisch, M.D.

War Activities: Participated in a project for the United States Navy of the Office of Scientific Research and Development under the direction of Dr. Steele . . . 1941-42

Military Service: Major, USA Medical Corps first on New Guinea and then Chief of Medical Service, Regional Hospital, Camp Shelby, Mississippi 1943-46

During 37 months of war service on official leave of absence from the University.

Member of:

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D

CURRICULUM VITAE

NAME:	Erwin N. Terry, M.D.	
ADDRESS:	R	
DATE AND PLACE OF BIRTH:	R Vienna, Austria	
MARITAL STATUS:	R	
EDUCATION:	Tel-Aviv High School of Commerce, Palestine	1940
	No. 7 Formation College	1945-46
	Medical Faculty of the University of the Saar	1951-56
MILITARY SERVICE:	Major, British Army and Israel Defense Forces	1941-46
FORMER APPOINTMENTS:	Moniteur, University of Saar, Department of Psychiatry	1954-56
	Civilian Contract Physician, P.A.C. Hospital, U.S. Air Force in Germany	1956-61
	Associate Medical Director, C.H. Boehringer Sohn, Ingelheim/Rhein, Germany	1961-63
PRESENT APPOINTMENTS:	Medical Director, Pharma Research Canada, Ltd., Pointe Clair, Quebec	1963-
	Research Fellow, New York University Research Service, Goldwater Memorial Hospital, Welfare Island, NY, NY	1964-
MEMBER OF:		

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Comprehensive Report

The Council for Tobacco Research

Walter Redisch, M.D.
Associate Professor of Clinical Medicine, New York University School of Medicine.
Research Associate, New York University Research Service, Goldwater Memorial Hospital

BLOOD FLOW STUDIES IN HYPERTENSIVE SMOKERS

This laboratory has studied vascular responses to cigarette smoking in man since 1955. There have been 4 phases of the investigation so far.

1) 1955 - 1959

In cooperation with Drs. Marion Sulzberger and Vincent Fontana it was first ascertained that in healthy volunteers the percentage of subjects with strongly positive reactions to skin testing with tobacco extract was about the same as the percentage of subjects who showed a significant decrease in blood flow response to cigarette smoking. The effects of cigarette smoking on blood flow in the lower extremity measured by plethysmography were then ascertained in 80 healthy subjects and correlated to other hemodynamic parameters as well as to the results of testing for skin sensitivity to tobacco extracts. Comparison with skin testing revealed on significant correlation: 90% of those who did not react to skin testing with tobacco extract had no decrease in peripheral blood flow in response to smoking.

2) 1959 - 1962

Since blood flow responses to smoking in the lower extremity seemed erratic, in that some test subjects showed unequivocal increase in total flow, it soon became evident that it was necessary to employ some acceptable means of separately estimating skin flow and muscle flow. A method of differential plethysmography has been developed in our laboratory on the basis of the rather constant difference between skin-mass/muscle mass ratio in the foot and in the leg. The formula following permits a rough estimation of skin and muscle flow by correcting for the most obvious errors.

$$Fl + Ff = F \text{ (c.c./min.)}$$
$$Vl + Vf = V \text{ (c.c.)}$$
$$P = \frac{F}{V} \text{ (c.c./100 c.c./min.)}$$

$$Ps = Pf + Cf\,\Delta \qquad Cf = 0.20$$
$$Pm = Pl - Cl\,\Delta \qquad Cl = 0.26$$
$$\Delta = \frac{Pf - Pl}{1 - Cf - Cl}$$

F = Flow Rate V = Volume
P = Perfusion Rate
L = Leg F = Foot S = Skin
M = Muscle C = Correction Factor

Of course, all experiments are done in the Constant Temperature Laboratory; the ones reported here were done at 25°C and 55% humidity.

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The Council for Tobacco Research

In order to be reasonably sure that the differences be meaningful, we considered as significant only changes of more than 1 1/2 ml. per 100 ml. of tissue/min.

At the present time 34 subjects have been tested with this method. There were 25 males and nine females. Their ages ranged from 24 to 87 years with an average of 56.3. Seven of the 34 subjects exhibited evidence of obliterative arteriosclerosis, while the rest had no demonstrable vascular disease. Nine of the group were significantly sensitive to one or more specific tobacco extracts. Skin and muscle flow responses of these 9 subjects were tested for the smoking of tobacco types to which their skin was sensitive.

		Skin Flow			Muscle Flow		
		Decrease	No Change	Increase	Decrease	No Change	Increase
Total Allergic	9	8	1	0	2	3	4
No OAS	8	7	1	0	2	2	4
OAS	1	1	0	0	0	1	0

In response to smoking, in eight of these nine tobacco-sensitive persons a significant decrease in skin blood flow was observed. One had a decrease not significant according to our criteria and was therefore listed as showing "no change"; none had an increase in skin flow.

		Skin Flow			Muscle Flow		
		Decrease	No Change	Increase	Decrease	No Change	Increase
Total Non-Allergic	25	2	15	8	2	12	11
No OAS	19	1	10	8	2	9	8
OAS	6	1	5	0	0	3	3

In contrast, of the 25 subjects who were skin negative, eight showed an increase in skin flow, 15 had no change and in only two a significant decrease in skin flow was observed.

There was no conclusive trend in muscle flow changes in either group. The differences in skin flow responses are highly significant.

3) 1962 - 1964

The study now turned to patients with non-gangerous occlusive atherosclerosis. 22 patients were studied in more than 100 experiments. The results

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were by and large identical with those in healthy subjects.

4) 1964 - 1967

The last phase of the project was devoted to a critical re-evaluation. The following conclusions were reached:

On the basis of studies carried out using segmental venous occlusion plethysmography "opthalmic artery pulsensor", capillaroscopy and photography and skin sensitivity testing for tobacco extracts, the following conclusions seem justified:

1) Vascular response to cigarette smoking in the lower extremity differs in skin and muscle. A decrease in skin perfusion is generally accompanied by an increase in muscle perfusion and vice versa.

2) Changes in relationship between skin and muscle perfusion depend quantitatively and qualitatively on environmental temperature.

3) At "neutral" temperatures between 22.5°C to 23.5°C., vascular responses to cigarette smoking are quantitatively at their lowest.

4) Whenever skin perfusion is decreased at 20°C following cigarette smoking, it will show an increase in response to cigarette smoking 25°C. Whenever muscle perfusion is increased in response to cigarette smoking at 20°C, it will decrease at 25°C in response to the same stimulus.

5) There is almost constant relationship between skin and muscle perfusion in vascular responses to smoking in the lower extremity. As a rule, increase in one is accompanied by a decrease in the other and vice versa.

6) Microcirculatory changes in response to tobacco smoking are dynamic in nature. The analysis of these changes require microcineamatography because of the rapid rate at which they occur.

7) "Opthalmic artery pulsensor" studies do not seem to be of value in assessing the response to smoking.

8) Skin sensitivity reaction to tobacco extracts may be dependent to a very large extent on preparation and composition of the extract.

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Total Essay of Proposal

BLOOD FLOW STUDIES IN HYPERTENSIVE SMOKERS

The effects of cigarette smoking on the peripheral circulation have been studied extensively in healthy subjects and in patients with arteriosclerosis. No reference could be found to a study of effects of cigarette smoking on blood-flow in patients with hypertension, untreated or under treatment with various substances.

In primary hypertension, the elevation of blood pressure is considered to be due to an increased peripheral resistance in the circulatory system. Until recently it was thought that cardiac output and stroke volume in primary hypertension are within normal limits. There was little or no evidence for over-activity of the sympathetic nervous system, vasoconstrictive reflexes remaining at normal levels. In the majority of cases catecholamine excretion, as a measure of sympathetic activity, was found to be within normal limits.

In the early labile stage of primary hypertension, some moderate elevation of catecholamine excretion has been shown in some cases. This elevation was particularly evident during peak elevations of blood pressure.

The whole concept of peripheral vascular resistance is ill defined. It has been shown that circulation in various organs or vascular beds may respond differently to a different stimulus. It has also been demonstrated that the ststus of a particular vascular bed, prior to stimulation, will influence the subsequent response. Observing vascular responses in one vascular bed does not necessarily permit the prediction of similar responses in other areas This concept of variability of vascular response in differing vascular beds would appear to contradict the concept of increase in total peripheral vascular resistance in essential hypertension.

A number of drugs currently in use to lower blood pressure affect catecholamine function in one way or another. Thus the question has been raised whether in primary hypertension one is basically dealing with an abnormality in catecholamine metabolism. Though it would appear that overall synthesis of catecholamines and their release from storage by neurone discharge as judged by urinary catecholamine excretions is normal, it has been shown that systemic blood vessels of subjects with hypertension are more reactive to catecholamines such as Norepinephrine than those of normals. This then, would suggest that the Norepinephrine released in response to nerve discharge is modulated differently. It has also been suggested that a defect of the storage mechanism of Norepinephrine, being smaller in hypertension compared to the normal, would lead to a greater response to infused or endogenous Norepinephrine as well will be absorbed, leaving more available for vasoconstriction. A third possibility to explain the increased vascular reactivity in primary hypertension has been suggested, namely insufficient tissue binding of exogenous or endogenous norepinephrine thus leading to an exaggerated vasoconstrictor response.

The pharmacologic action of nicotine consists of a primary transient stimulation and secondary more persistent depression of all sympathetic and parasympathetic ganglia. This includes the adrenal medulla and epinephrine

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is thereby discharged Nicotine and tobacco smoking have also been shown to exert an antidiuretic action. This effect is thought to be the result of stimulation of the supraoptical-hypophyseal system with the subsequent release of posterior pituitary anti-diuretic hormones.

Nicotine also markedly stimulates the central nervous system which is particularly evident for the respiratory and vasomotor centres of the medulla. Due to the multiple sites of action one may encounter initially a slowing of the heart rate due to stimulation of the central vagal nuclei and cardiac vagal ganglia. Later owing to stimulation of sympathetic ganglia, and the central vasomotor centre, tachycardia and a peripheral vasoconstriction may become prominent.

After the stage of sympathetic ganglionic stimulation is succeeded by paralysis, smaller vessels of the periphery, especially those of the skin, may dilate.

These combined effects of nicotine should be studied to ascertain the presence or absence of an increased catecholamine activity in the systemic blood vessels of patients with hypertension and the presence or absence of a basic abnormality in catecholamine metabolism in primary hypertension. Such findings in untreated patients with primary hypertension should be compared to findings in patients treated with various drugs to lower blood pressure. Also the effect of smoking on the treatment of hypertension with diuretics should be studied.

It is suggested that the effect of cigarette smoking be studied and compared in the following groups:

1) patients with primary hypertension who have not been treated before and are not being treated while the study is in progress

2) patients with primary hypertension treated with reserpine

3) patients with primary hypertension treated with thiazide

4) patients with a primary hypertension treated with a reserpine thiazide combination

5) patients with primary hypertension treated with guanethedin

6) normotensive subjects

Each group to consist of 5 subjects
Essential hypertension for the purposes of this study is defined as a sustained diastolic pressure of 100 mm Hg or higher without detectable underlying cause.

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Blood Flow Studies in Hypertensive Smokers

The method used in this study is differential venous occlusion plethysmography.

Plethysmographic measurements of the fot ad calf are taken, those of the foot being representative of skin blood flow while measurements of the calf are representative of muscle blood flow. The calf and foot are placed in the appropriate plethysmographic lucite chambers. The chambers are then made airtight with vaseline and foam rubber. Volume changes of the limb are calculated from the effect of a known volume, namely 5 ml air injected into the chamber, has on the deflection of the recorder. On the recording a time-scale permits measurement of the distance equivalent to 10 seconds on the base line. At this point a perpendicular is erected. Blood flow in ml/minute in 100 cc of tissue is calculated from the formula:

$$\frac{600 \times L}{K \times V} = \text{Blood Flow (ml per minute per 100 ml of tissue)}$$

L is the perpendicular rise of the slope in mm, during 10 seconds. K is the calibration constant of the recording apparatus in mm deflection per ml of change in volume. V is the volume of the enclosed calf or foot in ml which is determined by the water displacement overflow method. When measuring blood flow through the calf (i e. muscle vascular bed) two pressure cuffs are applied to the extremity to be measured. The distal (occlusion) cuff is inflated to 270 mm Hg, the one proximal to the plastic case (collecting cuff) to the individual's diastolic blood pressure minus 10 mm Hg. When measuring blood flow to the foot (i e. skin vascular bed) only the collecting cuff is used which is inflated to the individual's diastolic blood pressure minus 10 mm Hg. Following sudden occlusion, the linear portion of the rising slope of the recorded curve is used to calculate the rate of flow according to the formula mentioned above.

All experiments will of course be done in a constant temperature room, at temperatures of 20 and 28°C. Humidity to be held constant at 55%.

In order to avoid environmental influences, patients will be brought to the constant temperature laboratory where they will rest on a bed while quasi-continuously the skin temperature on both big toes and the right middle finger are recorded using a six channel Speedomax. A patient is considered to be adjusted to the environment of the room when the skin temperature of his toes and fingers has come down to constant room temperature and stayed there for thirty minutes. In patients whose skin temperature does not come down to room temperature despite prolonged exposure, maintenance of a constant skin temperature of toes and fingers for 30 minutes is considered to represent adaptation.

Walter Redisch, M.D.
New York University School of Medicine.

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